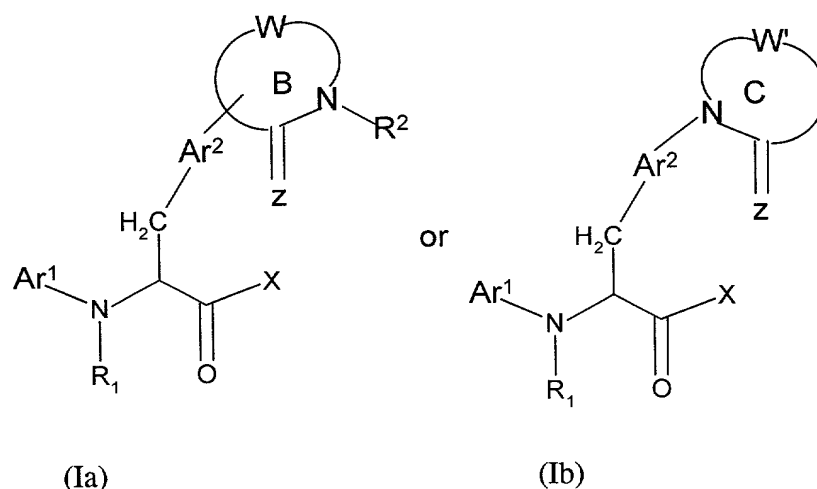


WHAT IS CLAIMED IS:

1. A compound (Ia) or (Ib):



wherein:

Ar¹ is an aryl, heteroaryl, cycloalkyl, or heterocyclic group wherein said aryl, heteroaryl, cycloalkyl, or heterocyclic group is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, -OS(O)₂-alkyl, -OS(O)₂-substituted alkyl, -OS(O)₂-

5 aryl, -OS(O)₂-substituted aryl, -OS(O)₂-heteroaryl, -OS(O)₂-substituted
heteroaryl, -OS(O)₂-heterocyclic, -OS(O)₂-substituted heterocyclic, -OSO₂-
NRR where each R is independently hydrogen or alkyl, -NRS(O)₂-alkyl, -
NRS(O)₂-substituted alkyl, -NRS(O)₂-aryl, -NRS(O)₂-substituted aryl, -
NRS(O)₂-heteroaryl, -NRS(O)₂-substituted heteroaryl, -NRS(O)₂-heterocyclic,
10 -NRS(O)₂-substituted heterocyclic, -NRS(O)₂-NR-alkyl, -NRS(O)₂-NR-
substituted alkyl, -NRS(O)₂-NR-aryl, -NRS(O)₂-NR-substituted aryl, -
NRS(O)₂-NR-heteroaryl, -NRS(O)₂-NR-substituted heteroaryl, -NRS(O)₂-NR-
heterocyclic, -NRS(O)₂-NR-substituted heterocyclic where R is hydrogen or
alkyl, -N[S(O)₂-R']₂ and -N[S(O)₂-NR']₂ where each R' is independently
15 selected from the group consisting of alkyl, substituted alkyl, aryl, substituted
aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted
heterocyclic;

R¹ is selected from the group consisting of hydrogen, alkyl, substituted
alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl,
20 cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl, heteroaryl,
substituted heteroaryl, heterocyclic and substituted heterocyclic;

Ar² is an aryl or heteroaryl group optionally substituted, in addition to
ring B or C, with one or two substituent(s) selected from the group consisting
of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, amino,
25 alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino,
acylamino, aminoacyl, N-acyl-N-alkylamino, substituted N-acyl-N-
alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-
(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino,
alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted
30 alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl,
cyano, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio,
substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl,
and substituted alkylsulfonyl;

Z is -O- or -S-;

05910702-072001
T00220"20207650

5 B is a group wherein W, together with $-C(=Z)NR^2-$, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and $-SO_n-$ (where n is 0 to 2) wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures
10 selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic, aryl and heteroaryl group to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of with one or two substituent(s) selected from the group consisting
15 of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, alkylene dioxy, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted
20 alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, nitro, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted
25 heteroaryl;

R² is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, and substituted cycloalkenyl;

30 C is a group wherein W', together with $-C(=Z)N-$, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and $-SO_n-$ (where n is 0 to 2) wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures

5 selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic,
aryl and heteroaryl group to form a bi- or tri-fused ring system and further
wherein said heterocyclic group and each of such ring structures are
optionally substituted with 1 to 3 substituents selected from the group
consisting of with one or two substituent(s) selected from the group consisting
10 of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, alkylenedioxy,
acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino,
dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-
acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino,
substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted
15 N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl,
substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted
cycloalkenyl, alkynyl, substituted alkynyl, cyano, nitro, acyl, substituted
acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio,
alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted
20 alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

X is selected from the group consisting of hydroxyl, alkoxy,
substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted
cycloalkoxy, cycloalkenoxy, substituted cycloalkenoxy, aryloxy, substituted
aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocycloxyloxy,
25 substituted heterocycloxyloxy and -NR^{''}R^{''} where each R^{''} is independently
selected from the group consisting of hydrogen, alkyl, substituted alkyl,
alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, aryl,
substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and
substituted heterocyclic;

30 and enantiomers, diastereomers and pharmaceutically acceptable salts
thereof;

and further wherein the compound of Formula I has a binding affinity to
VLA-4 as expressed by an IC₅₀ of about 15 μ M or less.

5 2. The compound of Claim 1 wherein (Ia), B is a group wherein W,
together with $-C(=Z)NR^2-$ where Z is $-O-$, forms an unsaturated heterocyclic
group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and
further the wherein the unsaturated heterocyclic group is optionally
substituted, in addition to the R^2 group, with 1 or 2 substituents selected from
10 the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy,
substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

15 3. The compound of Claim 1 wherein B is 2-pyridon-3-yl, 2-pyridon-4-yl,
or 6-pyrimidon-5-yl that is optionally substituted, in addition to the R^2 group,
with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy,
substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono
or dialkylamino.

20 4. The compound of Claim 1 wherein B is a group wherein W, together
with $-C(=Z)NR^2-$ where Z is $-O-$, forms a saturated or unsaturated
heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional
nitrogen atoms wherein said saturated or unsaturated heterocyclic group is
fused to a heterocyclic ring selected from the group consisting of dioxolane,
dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan,
25 oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-
dioxolan-2-one and wherein the resulting fused ring is optionally substituted,
in addition to the R^2 group, on any ring atom capable of substitution with 1 or
2 substituents selected from the group consisting of alkyl, alkoxy, substituted
alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or
30 dialkylamino.

5 5. The compound of Claim 1 wherein B is 2-pyridone or 6-pyrimidone that
is fused to a heterocyclic ring selected from the group consisting of
dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran,

5 furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-
dioxolan-2-one, and wherein the resulting fused ring is optionally substituted,
in addition to the R² group, on any ring atom capable of substitution with 1 or
2 substituents selected from the group consisting of alkyl, alkoxy, substituted
10 alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or
dialkylamino.

6. The compound of Claim 1 wherein Ar¹ is heteroaryl optionally
substituted with 1 to 3 substituents selected from the group consisting of
15 alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino,
cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl,
substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

7. The compound of Claim 6 wherein Ar¹ is 1-oxo-1,2,5-thiadiazole, 1,1-
dioxo-1,2,5-thiadiazole, pyridazine, pyrimidine or pyrazine ring which is
20 optionally substituted with 1 to 3 substituents selected from the group
consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino,
substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl,
heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and
halogen.

8. The compound of Claim 2 to 7 wherein Ar² is phenyl.

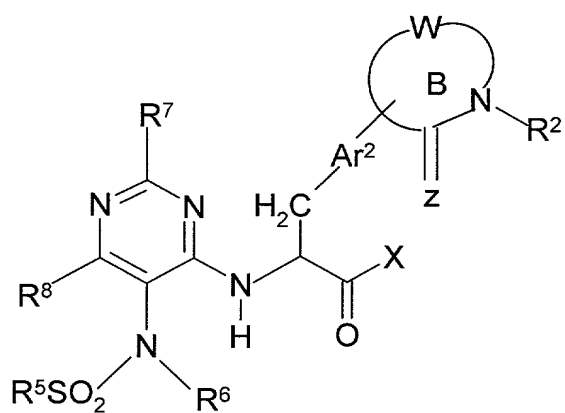
9. The compound of Claim 1 to 7 wherein X is hydroxyl and R¹ is
hydrogen.

10. The compound of Claim 8 wherein X is hydroxyl and R¹ is hydrogen.

11. The compound of Claim 1 wherein the compound has formula IIa, IIb,
IIc, IId, or IIe:

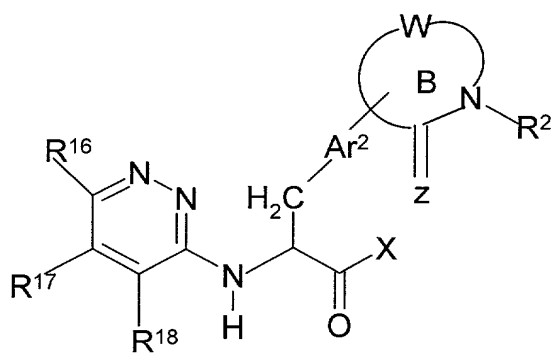
5

10



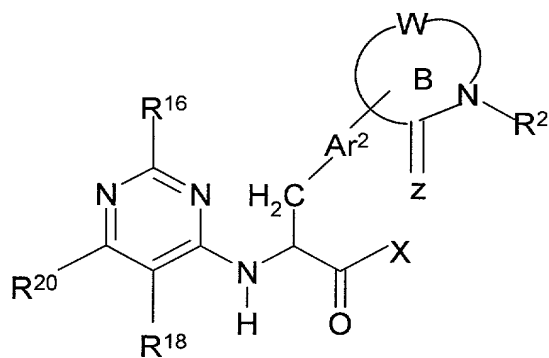
IIa

15



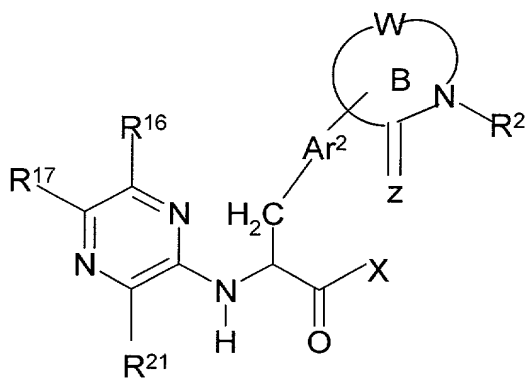
IIb

20



IIc

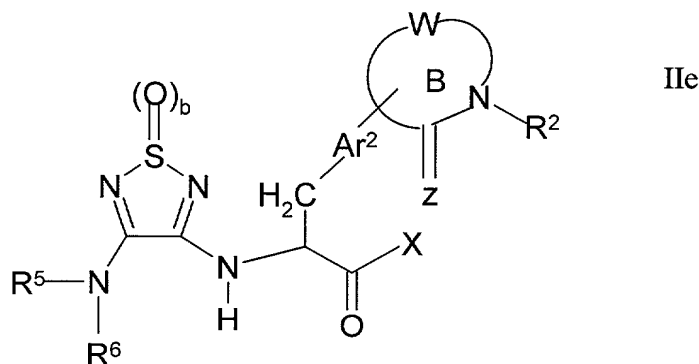
25



IIId

30

090220-20201660



wherein

X is hydroxyl or alkoxy;

Ar² is an aryl or heteroaryl group optionally substituted, in addition to ring B or C, with one or two substituent(s) selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, and substituted alkylsulfonyl;

R⁵ is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

5 R⁶ is selected from the group consisting of hydrogen, alkyl, substituted
alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted
cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl,
heteroaryl, substituted heteroaryl, and -SO₂R¹⁰ where R¹⁰ is selected from the
10 group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl,
cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic,
aryl, substituted aryl, heteroaryl, substituted heteroaryl;

 R⁷ and R⁸ are independently selected from the group consisting of
hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl,
substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted
15 heterocyclic and halogen;

 R¹⁶ and R¹⁷ are independently selected from the group consisting of
hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino,
substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl,
heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and
20 halogen; and

 R¹⁸ is selected from the group consisting of alkyl, substituted alkyl,
alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted
cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl,
heterocyclic and substituted heterocyclic;

25 R²⁰ is selected from the group consisting of hydrogen, alkyl, substituted
alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl,
substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted
heterocyclic and halogen;

 R²¹ is selected from the group consisting of alkyl, substituted alkyl,
30 alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted
cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2; and

 B is a group wherein W, together with -C(=Z)NR²-, forms a saturated or
unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4

5 additional heteroatoms selected from the group consisting of nitrogen,
oxygen, and $-\text{SO}_n-$ (where n is 0 to 2) wherein said saturated or unsaturated
heterocyclic group is optionally fused with one or two ring(s) structures
selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic,
aryl and heteroaryl group to form a bi- or tri-fused ring system and further
10 wherein said heterocyclic group and each of such ring structures are
optionally substituted with 1 to 3 substituents selected from the group
consisting of with one or two substituent(s) selected from the group consisting
of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy,
substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino,
15 substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-
alkylamino, substituted N-acyl-N-alkylamino, alkylene dioxy,
(alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-
alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted
alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl,
20 cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano,
acyl, substituted acyl, carboxy, substituted carboxy, nitro, thiol, alkylthio,
substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl,
substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted
heteroaryl;

25 R^2 is selected from the group consisting of alkyl, substituted alkyl, aryl,
substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted
cycloalkyl, cycloalkenyl, and substituted cycloalkenyl; and

and enantiomers, diastereomers and pharmaceutically acceptable salts
thereof.

30 12. The compound of Claim 11 wherein the compound is selected from
formula IIc, IId or IIe.

5 13. The compound of Claim 11 wherein B is a group wherein W, together
with -C(=Z)NR²- where Z is -O-, forms an unsaturated heterocyclic group
containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and
further the wherein the unsaturated heterocyclic group is optionally
substituted, in addition to the R² group, with 1 or 2 substituents selected from
10 the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy,
substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

14. The compound of Claim 13 wherein B is 2-pyridon-3-yl, 2-pyridon-4-yl,
or 6-pyrimidon-5-yl that is optionally substituted, in addition to the R² group,
15 with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy,
substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono
or dialkylamino.

15. The compound of Claim 11 wherein B is a group wherein W, together
20 with -C(=Z)NR²- where Z is -O-, forms a saturated or unsaturated
heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional
nitrogen atoms wherein said saturated or unsaturated heterocyclic group is
fused to a heterocyclic ring selected from the group consisting of dioxolane,
dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan,
25 oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-
dioxolan-2-one and wherein the resulting fused ring is optionally substituted,
in addition to the R² group, on any ring atom capable of substitution with 1 or
2 substituents selected from the group consisting of alkyl, alkoxy, substituted
alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or
30 dialkylamino.

16. The compound of Claim 15 wherein B is 2-pyridone or 6-pyrimidone that
is fused to a heterocyclic ring selected from the group consisting of
dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran,

5 furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-
dioxolan-2-one, and wherein the resulting fused ring is optionally substituted,
in addition to the R² group, on any ring atom capable of substitution with 1 or
2 substituents selected from the group consisting of alkyl, alkoxy, substituted
alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or
10 dialkylamino.

17. The compound of Claim 11 to 16 wherein Ar² is phenyl.

15 18. The compound of Claim 11 to 16 wherein X is hydroxyl and R¹ is
hydrogen.

19. The compound of Claim 18 wherein X is hydroxyl and R¹ is hydrogen.

20 20. A method for treating a disease mediated by VLA-4 in a patient, which
method comprises administering a pharmaceutical composition comprising a
pharmaceutically acceptable carrier and a therapeutically effective amount of
a compound of Claims 1 to 19.

25 21. A pharmaceutical composition comprising a pharmaceutically acceptable
carrier and a therapeutically effective amount of a compound of Claims 1-19.